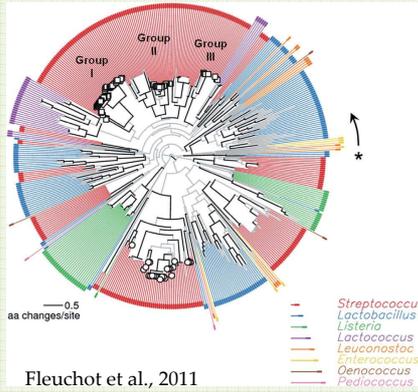


Background

Rgg-like proteins have been primarily identified and studied in streptococci as transcriptional regulators controlling the expression of genes encoding various functions. Recently, we showed that some of these regulators, in association with short hydrophobic peptides (SHP) playing the role of pheromones, are involved in a new quorum-sensing (QS) mechanism. The latter has been deciphered in detail in *Streptococcus thermophilus* where we showed that the activity of Rgg is directly controlled by a direct interaction with SHP.



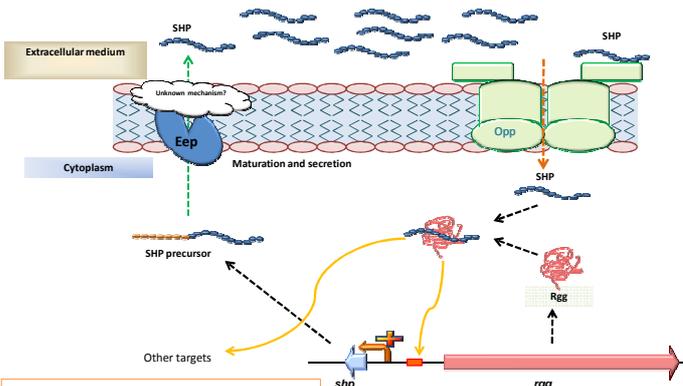
Fleuchot et al., 2011

The construction of a phylogenetic tree of all Rgg proteins found in Gram positive bacteria highlighted 68 shp/rgg systems only present in streptococci. They were classified into 3 groups using the following criteria: the amino acid sequence of SHP, and the genetic organisation of *shp* and *rgg* genes. We also identified a conserved Rgg DNA binding site specific to each SHP/Rgg groups. Furthermore, we have detected similar SHP/Rgg systems in different streptococci species, different SHP/Rgg systems in a streptococcus species and different SHP/Rgg inside a strain. These findings raised the question of cross-talk.

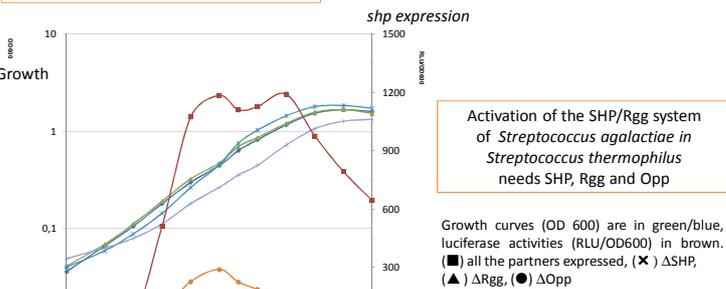
Results

SHP/Rgg systems function similarly in pathogen streptococci and in *Streptococcus thermophilus*

Similar mechanisms: a shared model in streptococci



An exported/imported peptide SHP activates a transcriptional regulator Rgg



Activation of the SHP/Rgg system of *Streptococcus agalactiae* in *Streptococcus thermophilus* needs SHP, Rgg and Opp

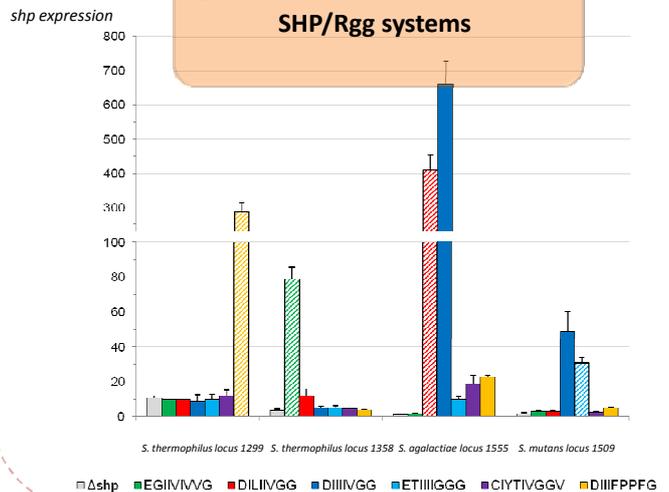
Growth curves (OD 600) are in green/blue, luciferase activities (RLU/OD600) in brown. (■) all the partners expressed, (X) ΔSHP, (▲) ΔRgg, (●) ΔOpp

Similar SHP mature peptide sequences identified in supernatants

(mature sequences in bold, except for stu_1299 in which the mature form remained unidentified; conserved acid aa is underlined)

Species	Locus	SHP sequence
<i>Streptococcus thermophilus</i> LMD9	ster_1358	MKKQILLTLLLVF EG IIVVVG
<i>Streptococcus thermophilus</i> LMD9	ster_1299	MKKVIAIFLFIQTVVV DII IFPPFG
<i>Streptococcus thermophilus</i> LMG13811	stu_0182	MKLLKIIVLLTCIYI IV GGV
<i>Streptococcus agalactiae</i>	gbs_1555	MKINKALLFTLIM DII LIVGG
<i>Streptococcus mutans</i>	smu.1509	MRNKIFMTLIVV LE TI III GGG

Evidence of cross-talk between SHP/Rgg systems



Similar genetic organisations in different shp/rgg loci



Conclusions-Perspectives

Search for SHP analogs, inhibitors of SHP/Rgg systems as a promising strategy to control bacterial functions

A new regulation mechanism via SHP/Rgg has been deciphered in streptococci.

SHP/Rgg might control virulence genes in pathogen streptococci (see David Perez's poster)

→ Identification of SHP/Rgg as a new target to control virulence in streptococci, potential basis of development of alternative to antibiotics

Reference

1. Fleuchot, B., et al., Rgg proteins associated with internalized small hydrophobic peptides: a new quorum-sensing mechanism in streptococci. Mol. Microbiol., 2011. 80: 1102-1119.